

CLAIMS

What is claimed is:

- 5           1. Nucleic acid molecules comprising a nucleic acid sequence that encodes  
an amino acid sequence wherein the amino acid sequence consists of the variable  
region of a monoclonal antibody that specifically binds to an extracellular domain of a  
*flt-1* receptor and neutralizes activation of the receptor.
- 10          2. The nucleic acid of claim 1, wherein the monoclonal antibody is  
produced by hybridoma cell line DC101 deposited as ATCC Accession No. HB 11534.
- 15          3. The nucleic acid of claim 1, wherein the monoclonal antibody is  
produced by hybridoma cell line M25.18A1 deposited as ATCC Accession No. HB  
12152.
- 20          4. The nucleic acid of claim 1, wherein the monoclonal antibody is  
produced by hybridoma cell line M73.24 deposited as ATCC Accession No. HB  
12153.
5. Nucleic acid molecules comprising a nucleic acid sequence that encodes  
an amino acid sequence wherein the amino acid sequence consists of the hypervariable  
region of a monoclonal antibody that specifically binds to an extracellular domain of a  
*flt-1* receptor and neutralizes activation of the receptor.

6        The nucleic acid of claim 5, wherein the monoclonal antibody is  
produced by hybridoma cell line DC101 deposited as ATCC Accession No. HB 11534.

7        The nucleic acid of claim 5, wherein the monoclonal antibody is  
5        produced by hybridoma cell line M25.18A1 deposited as ATCC Accession No. HB  
12152.

8        The nucleic acid of claim 5, wherein the monoclonal antibody is  
produced by hybridoma cell line M73.24 deposited as ATCC Accession No. HB  
10      12153.

9        A method for reducing tumor growth in a mammal in need thereof  
comprising treating the mammal with an effective amount of a monoclonal antibody  
which specifically binds to an extracellular domain of a *flt-1* receptor and reduces  
15      tumor growth.

10.      The method of claim 9, wherein the antibody is produced by a  
hybridoma cell line.

20      11.      The method of claim 10, wherein the hybridoma cell line is deposited as  
ATCC Accession No. HB 11534.

12 A method for reducing tumor growth in a mammal in need thereof comprising treating the mammal with an effective amount of a chimeric antibody which comprises an amino acid sequence of a human antibody constant region and an amino acid sequence of a non-human antibody variable region, and which specifically binds to an extracellular domain of a *flt-1* receptor and reduces tumor growth.

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13 The method of claim 12, wherein the non-human variable region is murine.

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14. A method for reducing tumor growth in a mammal in need thereof comprising treating the mammal with an effective amount of a humanized antibody which comprises amino acid sequences of variable framework and constant regions from a human antibody, and an amino acid sequence of a non-human antibody hypervariable region, and which specifically binds to an extracellular domain of a *flt-1* receptor and reduces tumor growth.

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15. The method of claim 14, wherein the amino acid sequence of the hypervariable region is murine.

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16. A method for inhibiting angiogenesis in a mammal in need thereof comprising treating the mammal with an effective amount of a monoclonal antibody which specifically binds to an extracellular domain of a *flt-1* receptor and inhibits angiogenesis.

17 The method of claim 16 wherein the antibody is produced by a  
hybridoma cell line

18 The method of claim 17, wherein the hybridoma cell line is deposited as  
5 ATCC Accession No. HB 11534.

19 A method for inhibiting angiogenesis in a mammal in need thereof  
comprising treating the mammal with an effective amount of a chimeric antibody which  
comprises an amino acid sequence of a human antibody constant region and an amino  
10 acid sequence of a non-human antibody variable region, and which specifically binds to  
an extracellular domain of a *flt-1* receptor and inhibits angiogenesis.

20 A method of claim 19, wherein the non-human variable region is  
murine.

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21. A method for inhibiting angiogenesis in a mammal in need thereof  
comprising treating the mammal with an effective amount of a humanized antibody  
which comprises amino acid sequences of variable framework and constant regions  
from a human antibody, and an amino acid sequence of a non-human antibody  
20 hypervariable region, and which specifically binds to an extracellular domain of a *flt-1*  
receptor and inhibits angiogenesis.

22 The method of claim 21, wherein the amino acid sequence of the  
hypervariable region is murine

23 The method of claim 21, wherein the hybridoma cell line is deposited as  
5 ATCC Accession No. HB 11534.

24 A method for reducing tumor growth in a mammal in need thereof  
comprising treating the mammal with an effective amount of a single chain antibody  
which specifically binds to an extracellular domain of a *flt-1* receptor and reduces  
10 tumor growth.

25 A method for inhibiting angiogenesis in a mammal in need thereof  
comprising treating the mammal with an effective amount of a single chain antibody  
which specifically binds to an extracellular domain of a *flt-1* receptor and inhibits  
15 angiogenesis

26. A single chain antibody that specifically binds to an extracellular domain  
of a *flt-1* receptor and neutralizes activation of the receptor.

20 27. A single chain antibody that specifically binds to an extracellular domain  
of a *flt-1* receptor and reduces tumor growth.

28. A single chain antibody that specifically binds to an extracellular domain  
of a *flt-1* receptor and inhibits angiogenesis.

29. A process for preparing a polypeptide that comprises an amino acid sequence that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor, the process comprising:

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of the variable region of a monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor; and

isolating the polypeptide from the cultured cells.

10 30. A process for preparing a polypeptide that comprises an amino acid sequence that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor, the process comprising:

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of the hypervariable region of a monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor; and

isolating the polypeptide from the cultured cells.

20 31. A process for preparing chimerized monoclonal antibodies that specifically bind to an extracellular domain of a *flt-1* receptor and neutralize activation of the receptor, the process comprising:

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of

- (i) a variable region of a monoclonal antibody of a mammal

5 other than a human wherein the variable region specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor, and

- (ii) a constant region of a human antibody; and isolating the chimerized monoclonal antibodies from the cultured cells.

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32. A process for preparing humanized monoclonal antibodies that specifically bind to an extracellular domain of a *flt-1* receptor and neutralize activation of the receptor, the process comprising:

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of:

(i) a hypervariable region of a monoclonal antibody of a mammal other than a human wherein the hypervariable region specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor,

15 (ii) a constant region of a human antibody, and

(iii) a variable region, other than the hypervariable region, substantially from a human antibody; and isolating the humanized monoclonal antibodies from the cultured cells.

33 A process for preparing a polypeptide that comprises an amino acid sequence that specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in a mammal, the process comprising  
culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of the variable region of a monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in the mammal; and  
isolating the polypeptide from the cultured cells.

10 34 A process for preparing a polypeptide that comprises an amino acid sequence that specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in a mammal, the process comprising  
culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence  
15 consists of the hypervariable region of a monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in the mammal;  
and  
isolating the polypeptide from the cultured cells.

20 35. A process for preparing chimerized monoclonal antibodies that specifically bind to an extracellular domain of a *flt-1* receptor and inhibit tumor growth in a recipient mammal, the process comprising:

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence consists of

- (i) a variable region of a monoclonal antibody of a mammal other than  
5 a human wherein the variable region specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in the recipient mammal, and  
(ii) a constant region of a human antibody; and isolating the chimerized monoclonal antibodies from the cultured cells.

10 36. A process for preparing humanized monoclonal antibodies that specifically bind to an extracellular domain of a *flt-1* receptor and inhibit tumor growth in a recipient mammal, the process comprising

culturing cells that express a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence wherein the amino acid sequence  
15 consists of.

- (i) a hypervariable region of a monoclonal antibody of a mammal other than a human wherein the hypervariable region specifically binds to an extracellular domain of a *flt-1* receptor and inhibits tumor growth in the recipient mammal,  
20 (ii) a constant region of a human antibody, and  
(iii) a variable region, other than the hypervariable region, substantially from a human antibody; and isolating the humanized monoclonal antibodies from the cultured cells.

37 A chimerized monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor.

38 A cell line producing the antibody of claim 37

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39 A composition comprising the antibody of claim 37 and a pharmaceutically acceptable carrier

40. The composition of claim 39 further comprising a chemotherapeutic  
10 agent and a pharmaceutically acceptable carrier

41 A chimerized monoclonal antibody that specifically binds to an  
extracellular domain of a *flt-1* receptor and reduces tumor growth.

15 42. A cell line producing the antibody of claim 41.

43. A composition comprising the antibody of claim 41 and a pharmaceutically acceptable carrier.

20 44. The composition of claim 43 further comprising a chemotherapeutic  
agent and a pharmaceutically acceptable carrier.

45 A humanized monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and neutralizes activation of the receptor

46 A cell line producing the antibody of claim 45

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47. A composition comprising the antibody of claim 45 and a pharmaceutically acceptable carrier

48. The composition of claim 47 further comprising a chemotherapeutic agent and a pharmaceutically acceptable carrier.

49. A humanized monoclonal antibody that specifically binds to an extracellular domain of a *flt-1* receptor and reduces tumor growth

15 50. A cell line producing the antibody of claim 49.

51. A composition comprising the antibody of claim 49 and a pharmaceutically acceptable carrier.

20 52. The composition of claim 51 further comprising a chemotherapeutic agent and a pharmaceutically acceptable carrier.